

**REMARKS/ARGUMENTS**

**Claim Rejections – 35 USC § 102**

Claims 1, 6, 10-11, 13 and 14 stand rejected under 35 USC 102(b) as being anticipated by deLearie (US 5,508,388). Applicant has amended claim 1 to expedite prosecution in the present invention. Support for claim 1 can be found on page 2, lines 23-28.

In view of the Examiner's point 5 made on page 2 of the Office Action dated October 2, 2007 ("Office Action"), Applicant has amended claim 1 by clearly adding the language "with the proviso that acetonitrile is not added to the reaction". Since Applicant has removed any addition of acetonitrile, Applicant now believes that claims 1, 6, 10-11, 13, and 14 are in condition for allowance and respectfully request that the Examiner's rejections for claims 1, 6, 10-11, 13, 14 under 35 USC 102(b) be withdrawn.

**Claim Rejections – 35 USC § 103**

Claims 1 to 16 stand rejected under 35 USC 103(a) as being unpatentable over Dazzi (US 3,660,388). Applicant has amended claim 1 of the present invention to remove any additions of acetonitrile to the reaction.

Before discussing the specific differences between the prior art and the present

invention, Applicant notes that “the prior art itself must provide a motivation or reason for the worker in the art, without the benefit of the Applicant’s specification, to make necessary changes in the reference device”. See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984).

Applicant was aware of the technology described by Dazzi prior to the present invention and directs the Examiner’s attention to page 1, lines 20 to 27 of the description in the present application (published international application WO 2005/058846). Dazzi uses 6.5 moles of pyridine per mole of DTPA as can be calculated from the amounts in grams in example 9, which Applicant holds as the closest description of this prior art. In relation to Dazzi, the present invention uses 6.0 moles or less of pyridine per mole of DTPA compared to 6.5 moles of pyridine per mole of DTPA. The information provided in example 9 of Dazzi further specifies conditions of the description in col. 1, lines 67 to 71 and also col. 2, line 68 to col. 3, line 8 of Dazzi and provides one skilled in the art with information on how to work the invention of Dazzi.

As discussed in the specification of the present application, it is known that pyridine is toxic and relatively expensive and that there has been a desire to reduce the amount of pyridine to a minimum, see page 2, lines 8 to 12 of the description (published international application WO 2005/058846). Furthermore the prior art taught one skilled in the art to use pyridine and similar toxic compounds to accelerate the reaction and improve yield. Specifically, as disclosed in Dazzi, that a tertiary nitrogen base or mixtures thereof, such as

pyridine or alkylated pyridines, should be added to the reaction since it is said to have the advantage to accelerate the reaction and improve the yield (col. 3, lines 2 to 6).

Applicant found that, unlike Dazzi, not only was it possible to reduce the amount of the toxic and expensive chemical pyridine, but the yield of DTPA-bis(anhydride) and the reaction rate could also be maintained at a surprisingly high level as demonstrated in examples 1 to 7 in the present application. This was wholly unexpected since the industry standard was to use about 10 molar amount of pyridine per mole of DTPA in industrial processing of DTPA bis(anhydride). No published art has indicated that it would be possible to reduce the amount of pyridine to be equal to or below the molar ratio of 6 times the molar amount of DTPA or even further without the addition of other non-desirable chemicals such as e.g. acetonitrile. Applicant respectfully points out here that it is well settled in the law that a reference must be considered not just for what it expressly teaches, but also for what it fairly suggests to one who is unaware of the claimed invention. *In re Baird*, 16 F.3d 380, (Fed. Cir. 1994). Furthermore, the present invention is not a mere discovery of optimum workable ranges by routine experimentation but represent a genuine step forward in this area of technology. Applicant therefore maintains that the present invention as claimed in claims 1 to 16 would not be obvious to one skilled in the art based on the teaching of Dazzi.

In view of the aforementioned paragraph it is clear that Dazzi teaches away from the present invention. 'Teaching away' simply means teaching a solution that would not lead to the claimed subject matter. As noted by the Federal Circuit:

A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).

*Para-Ordnance Mfg. v. SGS Importers Int'l*, 73 F.3d 1085 (Fed. Cir. 1995).

Dazzi does not teach, suggest, or disclose reducing the amount of pyridine to be equal to or below the molar ratio of 6 times the molar amount of DTPA or even further without the addition of other non-desirable chemicals such as e.g. acetonitrile.

Claims 1 to 16 stand rejected under 35 USC 103(a) as being unpatentable over Wagner (US 4,698,263).

Applicant was aware of the technology described by Wagner prior to the present invention and points the Examiner's attention to the paragraph joining pages 1 and 2 of the description of the present application (published international application WO 2005/058846). Wagner uses 7.5 moles of pyridine per mole of DTPA, see col. 12, lines 1 to 18. The ratio 7.5 is calculated from the amount is DTPA (100mmole) and the amounts of pyridine (60 ml which corresponds to 59 grams).

As discussed in the published international application WO 2005/058846 of the present application, it is known that pyridine is toxic and relatively expensive and that there

has been a desire to reduce the amount of pyridine to a minimum, see page 2, lines 8 to 27 of the description.

For the same arguments as used for Dazzi above, Applicant holds that the present invention does not teach, suggest, or disclose reducing the amount of pyridine to be equal to or below the molar ratio of 6 times the molar amount of DTPA or even further without the addition of other non-desirable chemicals such as e.g. acetonitrile. Therefore, Applicant respectfully points out that the present invention is not a mere discovery of optimum workable ranges by routine experimentation but represent a genuine step forward in this area of technology. Applicant therefore maintains that the present invention as claimed in claims 1 to 16 would not be obvious to one skilled in the art based on the teaching of Wagner.

Claims 1 to 16 stand rejected under 35 USC 103(a) as being unpatentable over Gibby (US 4,822,594).

As will be apparent from page 1, lines 29 to 32 of the description of the present application (published international application WO 2005/058846), Applicant was also aware of the technology described by Gibby prior to the present invention. Gibby uses 6.2 moles of pyridine per mole of DTPA, see the calculations presented above.

As discussed in the specification of the present application, at the time of this invention it was known that pyridine is toxic and relatively expensive and that there has been

a desire to reduce the amount of pyridine to a minimum, see page 2, lines 8 to 27 of the description.

For the same arguments as used for Dazzi and Wagner above, Applicant holds that Gibby does not teach, suggest, or disclose reducing the amount of pyridine to be equal to or below the molar ratio of 6 times the molar amount of DTPA or even further without the addition of other non-desirable chemicals such as e.g. acetonitrile. Therefore, Applicant respectfully points out that the present invention is not a mere discovery of optimum workable ranges by routine experimentation but represent a genuine step forward in this area of technology. Applicant therefore maintains that the present invention as claimed in claims 1 to 16 would not be obvious to the man skilled in the art based in the teaching of Gibby.

Claims 1 to 16 stand rejected under 35 USC 103(a) as being unpatentable over deLearie (US 5,508,388).

As will be apparent from page 2, lines 8 to 27 of the description of the present application (published international application WO 2005/058846), Applicant was also aware of the technology described by deLearie prior to the present invention. As explained above, deLearie wished to reduce the amount of pyridine in the production of DTPA-bis(anhydride) for the same reasons as the Applicant of the present invention, since pyridine is highly toxic and relatively expensive, see col. 3, lines 23 to 27 in the patent. It is also known that in the formation of DTPA-bis(anhydride) from DTPA and acetic acid anhydride, acetic acid produced must be neutralized with a base. Pyridine is considered as a preferred base since it

results in a high purity final product, see col. 2, lines 56 to 66. Applicant cannot see that deLearie in col. 2, lines 59-60 states anything about that [p]yridine is a particular active base that accelerates the reaction and improves the yield as the Examiner states. Applicant respectfully requests the Examiner point out where this is stated in deLearie. The accelerating properties of pyridine are however discussed by Dazzi as noted above and in the description of the present application. It was well known from the prior art that the amount of pyridine added in this reaction influences the reaction speed and also the purity of the product.

While deLearie reduced the amount of pyridine they also found that acetonitrile should be added as explained above. Applicant however wishes to reduce the amount of pyridine without the addition of further reactants and in particular to avoid the use of acetonitrile which is poisonous. Hence, Applicant with the present invention found that the amount of pyridine could be reduced to a molar amount of equal to or less than 6 times the molar amount of DTPA without addition of further reactants such as acetonitrile. The present invention therefore solves the reduction of addition of pyridine in an entirely different manner than does deLearie. deLearie nowhere indicates the solution reached to in the present invention. Applicant respectfully refers to *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984) wherein “the prior art itself must provide a motivation or reason for the worker in the art, without the benefit of the Applicant’s specification, to make necessary changes in the reference device”.

Unlike the present invention, deLearie reaches an entirely different solution. In view of the aforementioned paragraph, the teachings of the present invention reaches far beyond the mere discovery of optimum or workable ranges by routine experimentation. DeLearie provides no motivation or reason for one skilled in the art to make the necessary changes such as that in the present invention like reducing the amount of pyridine to be equal to or below the molar ratio of 6 times the molar amount of DTPA without adding to the reaction other non-desirable chemicals such as e.g. acetonitrile.

Applicant has in addition considered if the teachings in any combination of Dazzi and/or Wagner and/or Gibby and/or deLeari could be held to render the present invention obvious.

Assuming, *arguendo*, that the references are properly combinable, Applicant respectfully submits that any such combination would teach away from the present invention. All these prior art citations read on the reductions of pyridine to above the molar amount of 6 times the molar amount of DTPA and/or to include use of the additional reactant acetonitrile. Applicant therefore holds that none of the cited prior art in combination would render the present invention obvious over the prior art. Applicant therefore respectfully submits that claims 1 to 16 fulfill the requirements to overcome 35 USC 103(a).

In view of the foregoing favorable reconsideration of the claim rejections under 35 USC § 103 is respectfully requested.



**CONCLUSION**

In view of the amendments and remarks herein, Applicant believes that each ground for rejection made in the present application has been successfully overcome, and that all the pending claims, 1-16, are in condition for allowance.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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